## IN THE CLAIMS:

- 1. (ORIGINAL) A method for generating dopaminergic neurons comprising the steps of:
- (i) providing pluripotent cells;
- (ii) inhibiting one or more pathway components of a TGF-β signaling pathway in said pluripotent cells; and
- (iii) overexpressing one or more cell fate-inducing polypeptides in said pluripotent cells.
- 2. (ORIGINAL) The method of claim 1, wherein one of said cell fate-inducing polypeptides is Nurr-1.
- 3. (ORIGINAL) The method of claim 1, wherein one of said cell fate-inducing polypeptides is PTX3.
- 4. (ORIGINAL) The method of claim 1, wherein said cell fate-inducing polypeptides are Nurr-1 and PTX3.
- 5. (ORIGINAL) The method of claim 1, wherein said one or more cell fate-inducing polypeptides is overexpressed by:
  - (i) providing a polynucleotide encoding said cell fate-inducing polypeptide operably linked to a promoter; and
  - (ii) introducing said polynucleotide into said pluripotent cells under conditions suitable for expression of said polynucleotide.
- 6. (ORIGINAL) The method of claim 1, wherein said pluripotent cells are human pluripotent cells.
- 7. (ORIGINAL) The method of claim 1, wherein said pluripotent cells are mouse, rat, porcine, or non-human primate pluripotent cells.

Filed: December 9, 2003

O. Isacson, et al.

8. (ORIGINAL) The method of claim 6, wherein said pluripotent cells are embryonic

stem cells.

9. (ORIGINAL) The method of claim 1, wherein said TGF-β signaling pathway is the

Nodal signaling pathway.

10. (ORIGINAL) The method of claim 1, wherein said TGF-β. signaling pathway is the

Activin signaling pathway.

11. (ORIGINAL) The method of claim 1, wherein said TGF- $\beta$  signaling pathway is the

BMP2, BMP4, or BMP7 signaling pathway.

12. (ORIGINAL) The method of claim 1, wherein said TGF-β signaling pathway

component is selected from the group consisting of Nodal, Cryptic, Cripto, Activin, Activin

receptor I, Activin receptor II, Activin receptor IIb, TGF-β receptor, ALK-1, ALK-2, ALK-3,

ALK-4, ALK-6, ALK-7, BMP2, BMP4, BMP7, BMPRIa, BMPRIb, BMPRII, Smad2, Smad3,

Smad4, Smad5, and Smad6.

13. (ORIGINAL) The method of claim 1, wherein said TGF-β signaling pathway

component is Smad4.

14. (ORIGINAL) The method of claim 1, wherein said TGF-β. signaling pathway

component is Cripto.

15. (ORIGINAL) The method of claims 1, wherein said dopaminergic neurons are A9

dopaminergic neurons.

16. (ORIGINAL) The method of claim 1, wherein said pathway component is inhibited

by gene knockout of the nucleic acid encoding said component.

Filed: December 9, 2003

O. Isacson, et al.

17. (WITHDRAWN) The method of claim 1, wherein said pathway component is

inhibited by overexpressing small interfering RNA complementary to the mRNA encoding said

component in said pluripotent cells.

18. (WITHDRAWN) The method of claim 1, wherein said pathway component is

inhibited by overexpressing antisense oligonucleotide of the nucleic acid encoding said

component in said pluripotent cells.

19. (WITHDRAWN) The method of claim 1, wherein said pathway component is

inhibited by contacting said pluripotent cells with antibodies that specifically bind to said

pathway component.

20. (WITHDRAWN) The method of claim 1, wherein said pathway component is

inhibited by overexpressing a dominant negative version of said pathway component in said

pluripotent cells.

21. (WITHDRAWN) A method for treating a neurodegenerative disease in a patient, said

method comprising the steps of:

(i) providing dopaminergic neurons generated by a method comprising the steps of:

(a) providing pluripotent cells,

(b) inhibiting one or more pathway components of a TGF-β signaling pathway in

said pluripotent cells, and

(c) overexpressing one or more cell fate-inducing polypeptides in said

pluripotent cells; and

(ii) transplanting said dopaminergic neurons into the brain of said patient.

22. (WITHDRAWN) The method of claim 21, wherein said neurodegenerative disease is

Parkinson's disease.

Filed: December 9, 2003

O. Isacson, et al.

23. (WITHDRAWN) The method of claim 22, wherein said dopaminergic neurons are

transplanted into the caudate, the putamen, or the substantia nigra of said patient.

24. (WITHDRAWN) The method of claim 21, wherein one of said cell fate-inducing

polypeptides is Nurr-1.

25. (WITHDRAWN) The method of claim 21, wherein one of said cell fate-inducing

polypeptides is PTX3.

26. (WITHDRAWN) The method of claim 21, wherein said cell fate-inducing

polypeptides are Nurr-1 and PTX3.

27. (WITHDRAWN) The method of claim 21, wherein said one or more cell fate-

inducing polypeptides is overexpressed by:

(i) providing a polynucleotide encoding said cell fate-inducing polypeptide operably

linked to a promoter; and

ii) introducing said polynucleotide into said pluripotent cells under conditions suitable

for expression of said polynucleotide.

28. (WITHDRAWN) The method of claim 21, wherein said pluripotent cells are human

pluripotent cells.

29. (WITHDRAWN) The method of claim 21, wherein said pluripotent cells are mouse,

rat, porcine, or non-human primate pluripotent cells.

30. (WITHDRAWN) The method of claim 21, wherein said pluripotent cells are

embryonic stem cells.

31. (WITHDRAWN) The method of claim 21, wherein said TGF-β signaling pathway is

the Nodal signaling pathway.

Filed: December 9, 2003

O. Isacson, et al.

32. (WITHDRAWN) The method of claim 21, wherein said TGF-β signaling pathway is

the Activin signaling pathway.

33. (WITHDRAWN) The method of claim 21, wherein said TGF-β signaling pathway is

the BMP2, BMP4, or BMP7 signaling pathway.

34. (WITHDRAWN) The method of claim 21, wherein said TGF-β signaling pathway

component is selected from the group consisting of Nodal, Cryptic, Cripto, Activin, Activin

receptor I, Activin receptor II, Activin receptor IIb, TGF-β receptor, ALK-1, ALK-2, ALK-3,

ALK-4, ALK-6, ALK-7, BMP2, BMP4, BMP7, BMPRIa, BMPRIb, BMPRII, Smad2, Smad3,

Smad4, Smad5, and Smad6.

35. (WITHDRAWN) The method of claim 21, wherein said TGF-β signaling pathway

component is Smad4.

36. (WITHDRAWN) The method of claim 21, wherein said TGF-β signaling pathway

component is Cripto.

37. (WITHDRAWN) The method of claims 21, wherein said dopaminergic neurons are

A9 dopaminergic neurons.

38. (WITHDRAWN) The method of claim 21, wherein said pathway component is

inhibited by gene knockout of the nucleic acid encoding said component.

39. (WITHDRAWN) An isolated mammalian pluripotent cell expressing a recombinant

cell fate-inducing polypeptide and having a functional disruption of a TGF-β signaling pathway

component.

40. (WITHDRAWN) The cell of claim 39, wherein said cell is a human cell.

Filed: December 9, 2003

O. Isacson, et al.

41. (WITHDRAWN) The cell of claim 39, wherein said cell fate-inducing polypeptide is

Nurr-1 or PTX-3.

42. (WITHDRAWN) The cell of claim 39, wherein said functional disruption is a result

of a homozygous deletion of a gene encoding a TGF-β signaling pathway component.

43. (WITHDRAWN) The cell of claim 39, wherein said functional disruption is a result

of a missense mutation in a gene encoding TGF-β signaling pathway component.

44. (WITHDRAWN) The cell of claim 39, wherein said TGF-β signaling pathway

component is selected from the group consisting of Nodal, Cryptic, Cripto, Activin, Activin

receptor I, Activin receptor II, Activin receptor IIb, TGF-β receptor, ALK-1, ALK-2, ALK-3,

ALK-4, ALK-6, ALK-7, BMP2, BMP4, BMP7, BMPRIa, BMPRIb, BMPRII, Smad2, Smad3,

Smad4, Smad5, and Smad6.

45. (WITHDRAWN) The cell of claim 39, wherein said TGF-β signaling pathway

component is Smad4.

46. (WITHDRAWN) The cell of claim 39, wherein said TGF-β signaling pathway

component is Cripto.